

SEQUENCE LISTING

<110> Rosenblum et al.  
 <120> Immunotoxins Directed Against c-erbB-2 (HER-2/Neu)  
 Related Surface Antigens  
 <130> D5425CIP2  
 <140>  
 <141> 1999-05-26  
 <150> 08/404,499  
 <151> 1995-03-17  
 <160> 14



<210> 1  
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 <212> PRT  
 <213> Artificial Sequence  
 <220>  
 <223> synthetic linker sequence  
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Gly Gly Gly Gly Ser

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<210> 2  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence  
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 <223> Primer directed towards 5' upstream region of TAB 250  
 heavy chain  
 <400> 2

atatagcagg accatatg

18

<210> 3  
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 <212> DNA  
 <213> Artificial Sequence

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 <223> Primer directed towards coding region of TAb 250 heavy  
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 <400> 3  
 atgaacttgg ggctc 15  
  
 <210> 4  
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 <212> DNA  
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 <223> Primer directed towards 5' upstream region of TAb 250  
 light chain  
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 <210> 5  
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 light chain  
 <400> 5  
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 <210> 6  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence  
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 <223> Primer directed towards sFv-23  
 <400> 6  
 gctgcccaac cagccatggc gatgtctgac gtc 33  
  
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<211> 37  
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 <223> Primer directed towards sFv-23  
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 ccggagccac cgccaccgct agctgaggag actgtga 37

<210> 8  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence  
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 <223> Primer directed towards gelonin  
 <400> 8  
 ggtggcgggtg gctccggtct agataccggt agc 33

<210> 9  
 <211> 52  
 <212> DNA  
 <213> Artificial Sequence  
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 <223> Primer directed towards gelonin  
 <400> 9  
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<210> 10  
 <211> 1517  
 <212> DNA  
 <213> Artificial  
 <220>  
 <223> nucleotide sequence encoding scFv23-gelonin  
 immunotoxin  
 <400> 10  
 cccatggcga tgtctgacgt ccagctgacc cagtctccag caatcctgtc tgcattcca 60  
 ggggagaagg tcacaatgac ttgcagggcc accccaagtg taagttacat gcactggtat 120

cagcagaagc	caggatcctc	ccccaaacct	tggatttata	ccacatccaa	cctggcttct	180
ggagtccctg	ctcgcttcag	tggcgggtggg	tctgggacct	cttactctct	cacagcagca	240
gagtggaggc	tgaagatgct	gccacttatt	actgccagca	gtggagtcgt	agcccaccca	300
cgttcggagg	ggggtccaag	ctggaaataa	aaggttctac	ctctggttct	ggtaaattct	360
ctgaaggtaa	aggtgtgcag	ctgcaggagt	caggacctga	ggtggtgaag	cctggagggt	420
caatgaagat	atcctgcaag	acttctgggt	actcattcac	tggccacacc	atgaactggg	480
tgaagcagag	ccatggaaag	aaccttgagt	ggattggact	tattaatcct	tacaatggtg	540
atactaacta	caaccagaag	ttcaagggca	aggccacatt	tactgtagac	aagtcgtcca	600
gcacagccta	catggagctc	ctcagtctga	catctgagga	ctctgcagtc	tattactgtg	660
caaggagggt	tacggactgg	tacttcgatg	tctggggcgc	agggaccacg	gtcaccgtct	720
cctcagctag	cggtggcggt	ggctccggtc	tagataccgt	tagcttcagc	accaaaggcg	780
cgacctatat	cacctacgtt	aatttcctga	acgaactgcg	tgttaaactg	aaaccggaag	840
gtaacagcca	tggcatcccg	ctgctgcgta	aaggtgatga	cccgggtaaa	tgcttcgtgc	900
tggtggcgct	gagcaacgat	aacggtcagc	tggcagaaat	cgcaatcgat	gttaccagcg	960
tgtacgtagt	tggctatcag	gtgcgtaacc	gcagctactt	cttcaaagat	gctccggatg	1020
cagcgtacga	aggcctgttc	aaaaacacca	tcaaaaaccc	gctgctgttc	ggtggcaaaa	1080
ctcgtctgca	cttcgggtggc	agctatccga	gcctggaagg	cgaaaaagcg	taccgcgaaa	1140
ctaccgatct	gggtatcgaa	ccgctgcgca	tcggcatcaa	aaaactggac	gaaaacgcga	1200
tcgacaacta	caaaccgacc	gaaatcgcg	gctctctggt	tgtgatccag	atggtgagcg	1260
aagcggcacg	tttcaccttc	atcgaaaacc	agattcgtaa	caacttccag	cagcgtatcc	1320
gtccggcgaa	caacaacatc	tctctggaaa	acaaatgggg	caaactgagc	ttccagatcc	1380
gtaccagcgg	tgcgaacggt	atgttcagcg	aagcggtgga	actggaacgc	gcgaacggca	1440
aaaaataacta	cgtgactgcg	gtggatcagg	tgaaaccgaa	aatcgcactg	ctgaaattcc	1500
tcgagaaaga	cgagctg					1517

<210> 11

<211> 506

<212> PRT

<213> Artificial

<220>

<223> Polypeptide encoded by the scFv23-gelonin immunotoxin

<400> 11

Pro Met Ala Met Ser Asp Val Gln Leu Thr Gln Ser Pro Ala Ile

5

10

15

Leu	Ser	Ala	Ser	Pro	Gly	Glu	Lys	Val	Thr	Met	Thr	Cys	Arg	Ala	
				20					25					30	
Thr	Pro	Ser	Val	Ser	Tyr	Met	His	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	
				35					40					45	
Ser	Ser	Pro	Lys	Pro	Trp	Ile	Tyr	Thr	Thr	Ser	Asn	Leu	Ala	Ser	
				50					55					60	
Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Gly	Gly	Ser	Gly	Thr	Ser	Tyr	
				65					70					75	
Ser	Leu	Thr	Val	Ser	Arg	Val	Glu	Ala	Glu	Asp	Ala	Ala	Thr	Tyr	
				80					85					90	
Tyr	Cys	Gln	Gln	Trp	Ser	Arg	Ser	Pro	Pro	Thr	Phe	Gly	Gly	Gly	
				95					100					105	
Ser	Lys	Leu	Glu	Ile	Lys	Gly	Ser	Thr	Ser	Gly	Ser	Gly	Lys	Ser	
				110					115					120	
Ser	Glu	Gly	Lys	Gly	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Glu	Val	
				125					130					135	
Val	Lys	Pro	Gly	Gly	Ser	Met	Lys	Ile	Ser	Cys	Lys	Thr	Ser	Gly	
				140					145					150	
Tyr	Ser	Phe	Thr	Gly	His	Thr	Met	Asn	Trp	Val	Lys	Gln	Ser	His	
				155					160					165	
Gly	Lys	Asn	Leu	Glu	Trp	Ile	Gly	Leu	Ile	Asn	Pro	Tyr	Asn	Gly	
				170					175					180	
Asp	Thr	Asn	Tyr	Asn	Gln	Lys	Phe	Lys	Gly	Lys	Ala	Thr	Phe	Thr	
				185					190					195	

Val	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr	Met	Glu	Leu	Leu	Ser	Leu	200	205	210
Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Arg	Val	Thr	215	220	225
Asp	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Ala	Gly	Thr	Thr	Val	Thr	Val	230	235	240
Ser	Ser	Ala	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Leu	Asp	Thr	Val	Ser	245	250	255
Phe	Ser	Thr	Lys	Gly	Ala	Thr	Tyr	Ile	Thr	Tyr	Val	Asn	Phe	Leu	260	265	270
Asn	Glu	Leu	Arg	Val	Lys	Leu	Lys	Pro	Glu	Gly	Asn	Ser	His	Gly	275	280	285
Ile	Pro	Leu	Leu	Arg	Lys	Gly	Asp	Asp	Pro	Gly	Lys	Cys	Phe	Val	290	295	300
Leu	Val	Ala	Leu	Ser	Asn	Asp	Asn	Gly	Gln	Leu	Ala	Glu	Ile	Ala	305	310	315
Ile	Asp	Val	Thr	Ser	Val	Tyr	Val	Val	Gly	Tyr	Gln	Val	Arg	Asn	320	325	330
Arg	Ser	Tyr	Phe	Phe	Lys	Asp	Ala	Pro	Asp	Ala	Ala	Tyr	Glu	Gly	335	340	345
Leu	Phe	Lys	Asn	Thr	Ile	Lys	Asn	Pro	Leu	Leu	Phe	Gly	Gly	Lys	350	355	360
Thr	Arg	Leu	His	Phe	Gly	Gly	Ser	Tyr	Pro	Ser	Leu	Glu	Gly	Glu	365	370	375

Lys	Ala	Tyr	Arg	Glu	Thr	Thr	Asp	Leu	Gly	Ile	Glu	Pro	Leu	Arg	380	385	390
Ile	Gly	Ile	Lys	Lys	Leu	Asp	Glu	Asn	Ala	Ile	Asp	Asn	Tyr	Lys	395	400	405
Pro	Thr	Glu	Ile	Ala	Ser	Ser	Leu	Val	Val	Ile	Gln	Met	Val	Ser	410	415	420
Glu	Ala	Ala	Arg	Phe	Thr	Phe	Ile	Glu	Asn	Gln	Ile	Arg	Asn	Asn	425	430	435
Phe	Gln	Gln	Arg	Ile	Arg	Pro	Ala	Asn	Asn	Asn	Ile	Ser	Leu	Glu	440	445	450
Asn	Lys	Trp	Gly	Lys	Leu	Ser	Phe	Gln	Ile	Arg	Thr	Ser	Gly	Ala	455	460	465
Asn	Gly	Met	Phe	Ser	Glu	Ala	Val	Glu	Leu	Glu	Arg	Ala	Asn	Gly	470	475	480
Lys	Lys	Tyr	Tyr	Val	Thr	Ala	Val	Asp	Gln	Val	Lys	Pro	Lys	Ile	485	490	495
Ala	Leu	Leu	Lys	Phe	Leu	Glu	Lys	Asp	Glu	Leu					500	505	

<210> 12

<211> 1500

<212> DNA

<213> Artificial

<220>

<223> nucleotide sequence encoding scFv23-gelonin  
immunotoxin

<400> 12

atgagtgacg	tccagctgac	ccagtctcca	gcaatcctgt	ctgcatctcc	aggggagaag	60
gtcacaatga	cttgcagggc	cacccaagt	gtaagttaca	tgcactggta	tcagcagaag	120
ccaggatcct	cccccaaacc	ttggatttat	accacatcca	acctggcttc	tggagtcctt	180
gctcgcttca	gtggcggtgg	gtctgggacc	tcttactctc	tcacagtcag	cagagtgagg	240
gctgaagatg	ctgccactta	ttactgccag	cagtggagtc	gtagcccacc	cacgttcgga	300
gggggggtcca	agctggaaat	aaaaggttct	acctctgggt	ctggtaaata	ttctgaaggt	360
aaagggtgtgc	agctgcagga	gtcaggacct	gaggtggtga	agcctggagg	ttcaatgaag	420
atatcctgca	agacttctgg	ttactcattc	actggccaca	ccatgaactg	ggtgaagcag	480
agccatggaa	agaaccttga	gtggattgga	cttattaata	cttacaatgg	tgataactaa	540
tacaaccaga	agttcaaggg	caaggccaca	tttactgtag	acaagtcgtc	cagcacagcc	600
tacatggagc	tcctcagtct	gacatctgag	gactctgcag	tctattactg	tgcaaggagg	660
gttacggact	ggtacttcga	tgtctggggc	gcagggacca	cggtcaccgt	ctcctcagct	720
agcgggtggcg	gtggctccgg	tctagacacc	gtgagcttta	gcactaaagg	tgccacttat	780
attacctacg	tgaatttctt	gaatgagcta	cgagttaaata	tgaaacccga	aggtaacagc	840
catggaatcc	cattgctgcg	caaaaaatgt	gatgatcctg	gaaagtgttt	cgttttggtta	900
gcgctttcaa	atgacaatgg	acagttggcg	gaaatagcta	tagatgttac	aagtgtttat	960
gtggtgggct	atcaagtaag	aaacagatct	tacttcttta	aagatgctcc	agatgctgct	1020
tacgaaggcc	tcttcaaaaa	cacaattaaa	acaagacttc	attttggcgg	cagctatccc	1080
tcgctggaag	gtgagaaggc	atatagagag	acaacagact	tgggcattga	accattaagg	1140
attggcatca	agaaacttga	tgaaaatgcg	atagacaatt	ataaaccaac	ggagatagct	1200
agttctctat	tggttggtat	tcaaatggtg	tctgaagcag	ctcgattcac	ctttattgag	1260
aaccaaatga	gaaataactt	tcaacagaga	attcgcccgg	cgaataatac	aatcagcctt	1320
gagaataaat	ggggtaaact	ctcgttccag	atccggacat	caggtgcaaa	tggaatgttt	1380
tcggaggcag	ttgaattgga	acgtgcaaat	ggcaaaaaat	actatgtcac	cgcagttgat	1440
caagtaaaac	ccaaaatagc	actcttgaag	ttcgtcgata	aagatcctaa	agcttaatga	1500

<210> 13

<211> 498

<212> PRT

<213> Artificial

<220>

<223> Polypeptide encoded by the scFv23-gelonin immunotoxin

<400> 13

Met Ser Asp Val Gln Leu Thr Gln Ser Pro Ala Ile Leu Ser Ala

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10

15



Ser	Pro	Gly	Glu	Lys	Val	Thr	Met	Thr	Cys	Arg	Ala	Thr	Pro	Ser	20	25	30
Val	Ser	Tyr	Met	His	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Ser	Ser	Pro	35	40	45
Lys	Pro	Trp	Ile	Tyr	Thr	Thr	Ser	Asn	Leu	Ala	Ser	Gly	Val	Pro	50	55	60
Ala	Arg	Phe	Ser	Gly	Gly	Gly	Ser	Gly	Thr	Ser	Tyr	Ser	Leu	Thr	65	70	75
Val	Ser	Arg	Val	Glu	Ala	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	80	85	90
Gln	Trp	Ser	Arg	Ser	Pro	Pro	Thr	Phe	Gly	Gly	Gly	Ser	Lys	Leu	95	100	105
Glu	Ile	Lys	Gly	Ser	Thr	Ser	Gly	Ser	Gly	Lys	Ser	Ser	Glu	Gly	110	115	120
Lys	Gly	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Glu	Val	Val	Lys	Pro	125	130	135
Gly	Gly	Ser	Met	Lys	Ile	Ser	Cys	Lys	Thr	Ser	Gly	Tyr	Ser	Phe	140	145	150
Thr	Gly	His	Thr	Met	Asn	Trp	Val	Lys	Gln	Ser	His	Gly	Lys	Asn	155	160	165
Leu	Glu	Trp	Ile	Gly	Leu	Ile	Asn	Pro	Tyr	Asn	Gly	Asp	Thr	Asn	170	175	180
Tyr	Asn	Gln	Lys	Phe	Lys	Gly	Lys	Ala	Thr	Phe	Thr	Val	Asp	Lys	185	190	195

Ser	Ser	Ser	Thr	Ala	Tyr	Met	Glu	Leu	Leu	Ser	Leu	Thr	Ser	Glu
				200					205					210
Asp	Ser	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Arg	Val	Thr	Asp	Trp	Tyr
				215					220					225
Phe	Asp	Val	Trp	Gly	Ala	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala
				230					235					240
Ser	Gly	Gly	Gly	Gly	Ser	Gly	Leu	Asp	Thr	Val	Ser	Phe	Ser	Thr
				245					250					255
Lys	Gly	Ala	Thr	Tyr	Ile	Thr	Tyr	Val	Asn	Phe	Leu	Asn	Glu	Leu
				260					265					270
Arg	Val	Lys	Leu	Lys	Pro	Glu	Gly	Asn	Ser	His	Gly	Ile	Pro	Leu
				275					280					285
Leu	Arg	Lys	Lys	Cys	Asp	Asp	Pro	Gly	Lys	Cys	Phe	Val	Leu	Val
				290					295					300
Ala	Leu	Ser	Asn	Asp	Asn	Gly	Gln	Leu	Ala	Glu	Ile	Ala	Ile	Asp
				305					310					315
Val	Thr	Ser	Val	Tyr	Val	Val	Gly	Tyr	Gln	Val	Arg	Asn	Arg	Ser
				320					325					330
Tyr	Phe	Phe	Lys	Asp	Ala	Pro	Asp	Ala	Ala	Tyr	Glu	Gly	Leu	Phe
				335					340					345
Lys	Asn	Thr	Ile	Lys	Thr	Arg	Leu	His	Phe	Gly	Gly	Ser	Tyr	Pro
				350					355					360
Ser	Leu	Glu	Gly	Glu	Lys	Ala	Tyr	Arg	Glu	Thr	Thr	Asp	Leu	Gly
				365					370					375

Ile Glu Pro Leu Arg Ile Gly Ile Lys Lys Leu Asp Glu Asn Ala  
380 385 390

Ile Asp Asn Tyr Lys Pro Thr Glu Ile Ala Ser Ser Leu Leu Val  
395 400 405

Val Ile Gln Met Val Ser Glu Ala Ala Arg Phe Thr Phe Ile Glu  
410 415 420

Asn Gln Ile Arg Asn Asn Phe Gln Gln Arg Ile Arg Pro Ala Asn  
425 430 435

Asn Thr Ile Ser Leu Glu Asn Lys Trp Gly Lys Leu Ser Phe Gln  
440 445 450

Ile Arg Thr Ser Gly Ala Asn Gly Met Phe Ser Glu Ala Val Glu  
455 460 465

Leu Glu Arg Ala Asn Gly Lys Lys Tyr Tyr Val Thr Ala Val Asp  
470 475 480

Gln Val Lys Pro Lys Ile Ala Leu Leu Lys Phe Val Asp Lys Asp  
485 490 495

Pro Lys Ala

<210> 14

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> 212 Linker (synthetic linker sequence)

<400> 14

A'  
CONCL'D.

Gly Ser Thr Ser Gly Ser Gly Lys Ser Ser Glu Gly Lys Gly

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